EXHIBIT B

Form Approved Through 05/2004
OMB No. 0925-0001

Department of Health and Human Services
Public Health Services

Grant Application

Follow instructions carefully.
Do not exceed 56-character length restrictions, including spaces.

LEAVE BLANK—FOR PHS USE ONLY.		
Type	Activity	Number
Review Group		Formerly
Council/Board (Month, Year)		Date Received

1. TITLE OF PROJECT
Development of a Massed Practice Stroke Therapy Device

2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION ☒ NO ☐ YES
(If "Yes," state number and title)
Number: Title:

3. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR — **New Investigator** ☒ No ☐ Yes

3a. NAME *(Last, first, middle)*: Koeneman, James, Bryant

3b. DEGREE(S): BSME MS PhD

3c. POSITION TITLE: President

3d. MAILING ADDRESS *(Street, city, state, zip code)*: 1949 East Broadway Road, Tempe, AZ 85282

3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT:

3f. MAJOR SUBDIVISION:

3g. TELEPHONE AND FAX *(Area code, number and extension)*
TEL: (480)557-0448 FAX: (480) 557-0449

E-MAIL ADDRESS: jbk@btic.com

4. HUMAN SUBJECTS RESEARCH ☐ No ☒ Yes

4a. Research Exempt ☒ No ☐ Yes
If "Yes," Exemption No.

4b. Human Subjects Assurance No.: None

4c. NIH-defined Phase III Clinical Trial ☒ No ☐ Yes

5. VERTEBRATE ANIMALS ☒ No ☐ Yes

5a. If "Yes," IACUC approval Date

5b. Animal welfare assurance no

6. DATES OF PROPOSED PERIOD OF SUPPORT *(month, day, year—MM/DD/YY)*		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD		8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT	
From	Through	7a. Direct Costs ($)	7b. Total Costs ($)	8a. Direct Costs ($)	8b. Total Costs ($)
07/15/02	01/15/03	$100,000	$100,000	$100,000	$100,000

9. APPLICANT ORGANIZATION
Name: Kinetic Muscles, Inc.
Address: 1949 East Broadway Road, Tempe, AZ 85282

Institutional Profile File Number (if known)

10. TYPE OF ORGANIZATION
Public: → ☐ Federal ☐ State ☐ Local
Private: → ☐ Private Nonprofit
For-profit: → ☐ General ☒ Small Business
☐ Woman-owned ☐ Socially and Economically Disadvantaged

11. ENTITY IDENTIFICATION NUMBER
EIN 86-1031432
DUNS NO. *(if available)*

Congressional District 1

12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE
Name: Jame B. Koeneman
Title: President
Address: 1949 East Broadway Road, Tempe, AZ 85282
Tel (480) 557-0448 FAX (480) 55-0449
E-Mail: jbk@btic.com

13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION
Name: James B. Koeneman
Title: President
Address: 1949 East Broadway Road, Tempe, AZ 85282
Tel (480) 557-0448 FAX (480) 557-0449
E-Mail: jbk@btic.com

14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

SIGNATURE OF PI/PD NAMED IN 3a. *(In ink. "Per" signature not acceptable.)* James B Koeneman — DATE 11/30/01

15. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF OFFICIAL NAMED IN 13. *(In ink. "Per" signature not acceptable.)* James B Koeneman — DATE 11/30/01

DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information. **DO NOT EXCEED THE SPACE PROVIDED.**

Stroke (CVA) is the leading cause of disability in the United States and it is estimated that its prevalence will more than double over the next 50 years. Current stroke therapy is labor-intensive and costly. The United States spends $17 billion taking care of stroke survivors. Recently, concentrated, massed practice therapies have been developed that improve function in CVA patients by reversing the effects of "learned nonuse". The objective of this project is to investigate the feasibility of a device that facilitates the administration of massed practice stroke therapy. The long-term objective is to provide a lightweight device for home use that provides motion and biofeedback of desired and undesireable muscle activity. Software controls the function of the device and monitors patient progress and compliance. A pneumatic artificial muscle will be used to provide physical motion. This artificial muscle has many of the properties of human muscle. It is lightweight, flexible and has spring like properties. This project will focus on treating wrist extensor weakness, however, the concept applies to all areas affected by motor impairment.

PERFORMANCE SITE(S) *(organization, city, state)*
Kinetic Muscles, Inc. Tempe, AZ
Barrow Neurological Institute at St. Joeseph's Hospital and Medical Center, Phoenix, AZ

KEY PERSONNEL. See instructions. *Use continuation pages as needed* to provide the required information in the format shown below.
Start with Principal Investigator. List all other key personnel in alphabetical order, last name first.

Name	Organization	Role on Project
Koeneman, James B.	Kinetic Muscles, Inc.	P.I.
Eblen, Cristobel	Southwest Behavioral Health Center	Statistical Consultant
Herring, Donald	Arizona State University	Human Factors, Indus Des.
Koeneman, Edward	Kinestic Muscles, Inc.	Device design & fabrication
Kwasnica, Christina	Barrows Neurological Institue	Physician evaluation
Wendelboe, Douglas	Kinetic Muscles, Inc.	Software & firmware design
Wolf, Steven	Emory University	Therapy concultant

Disclosure Permission Statement. Applicable to SBIR/STTR Only. See instructions. ☒ **Yes** ☐ No

• Principal Investigator/Program Director (Last, first, middle): Koeneman, James Bryant

The name of the principal investigator/program director must be provided at the top of each printed page and each continuation page.

Type density and size must conform to limits and specifications provided in the PHS 398 Instructions.

RESEARCH GRANT

TABLE OF CONTENTS

* SBIR/STTR Phase I applications: Items A-D of the Research Plan are limited to 15 pages.

Appendix *(Five collated sets. No page numbering necessary for Appendix.)*

Check if Appendix is Included ☐

Appendices NOT PERMITTED for Phase I SBIR/STTR unless specifically solicited.

Number of publications and manuscripts accepted for publication *(not to exceed 10)* _____

Other items (list):

EXHIBIT B

Principal Investigator/Program Director *(Last, first, middle)*: Koeneman, James, Bryant

BUDGET JUSTIFICATION PAGE MODULAR RESEARCH GRANT APPLICATION				
Initial Budget Period	**Second Year of Support**	**Third Year of Support**	**Fourth Year of Support**	**Fifth Year of Support**
$ 100,000.00	$	$	$	$
Total Direct Costs Requested for Entire Project Period				$ 100,000.00

Personnel

During the 6 months of this project, the P.I. will have 30% effort. He will coordinate activities, manage the budget and provide biomechanical analysis. Edward Koeneman will have 30% effort during the 6 months. He will be responsible for hardware design, test and assembly of the devices to be used in the pilot study. Douglas Wendelboe will have 30% effort during the 6 months of the project and will be responsible for programming and data retrieval.

Consortium

Dr. Kwasnica's clinical practice will coordinate the patient recruitment and patient evaluation. The estimated costs are $13,500. The clinical measurements in the Barrow Neurological Clinic at St. Joseph's Medical Center are estimated to cost $12,500. The statistical consulting of Dr. Eblen plus the Human Factors consulting of Donald Herring plus the neuro rehabilitation theory consulting of Dr. He are estimated to be $3,300. Dr. Steven Wolf from Emory University will consult on concentrated practice, therapy protocols, and evaluation of results at no cost to the grant.

Fixed Fee (SBIR/STTR Only)
None

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
James B. Koeneman	Senior Biomechanics Consultant

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Minnesota, Minneapolis, MN	BSME	1959	Mechanical Engineering
Case Western Reserve University, Cleveland, OH	MS	1966	Bioengineering
Case Western Reserve University, Cleveland, OH	PhD	1970	Structures/Mechanical Design

RESEARCH AND PROFESSIONAL EXPERIENCE

1994 - present	Senior Bioengineering Consultant, BTI Consultants, Tempe, AZ. Assistive Devices, Biomechanics, Development of Composite Materials, Stress Analysis, Failure Analysis.
1994 - 1998	V.P. of Engineering, Orthologic Corporation, Tempe, AZ. Fracture fixation devices, bone growth stimulators.
1984 - 1994	Head of Bioengineering Division, Harrington Arthritis Research Center, Phoenix, AZ. Development of assistive devices, orthopedic implant design and testing, finite element analyses.
1981 - 1983	President, Paulson Medical Devices, Inc., Erie, PA. Development of fracture fixation devices and orthopedic implants.
1974 - 1981	Head of Bioengineering Division, Lord Corporation, Erie, PA. Development and manufacture of orthopedic implants. Composite material development.
1970 - 1974	Bell Telephone Laboratories, Columbus, OH. Development of Piezoelectric switching devices.
1960 - 1964	Reactor Engineer, U.S. Atomic Energy Commission, Argonne, IL.
1959 - 1960	Reactor Engineer, Argonne National Laboratory, Idaho Falls, ID.

PUBLICATIONS

Recipient of 16 patents, co-author of 22 publications and over 115 presentations at technical society meetings. Seven relevant publications listed below:

J.B. Koeneman and J.S. Kaiser, "A Functional Evaluation of the DataHand® Key Entry System User Experience Evaluated By Questionnaire," RESNA, 1994.

J.B. Koeneman and C. Eblen, "A Longitudinal Evaluation of Four-Wheeled Walker: Effects of Experience," Topics in Geriatric Rehabilitation, 8(3)3, 1993.

J.B. Koeneman, "Advanced Materials for Assistive Devices," Topics in Geriatric Rehabilitation, Vol. 8, No. 2, December 1992.

J.B. Koeneman, with others, "A Multi-Dimensional Evaluation of a Four-Wheeled Walker," Assistive Technology, Vol. 4, No. 1, 1992.

J.B. Koeneman, N. Reich, P. Otten, and J. Kaiser, "Clothing for Special Needs; An Information Arena," 10th Annual RESNA Conference, San Jose, CA, 1987.

J.B. Koeneman and M. Phillips, "Composite Materials for Rehabilitation Devices," 10th Annual RESNA Conference, San Jose, CA, 1987.

J.B. Koeneman, "State of the Art of Finite Element Analysis in Orthopaedics," Materials Research Society, Proceedings of Medical Devices and Materials Symposium, 1987.

AWARDS

International Fellow of Biomaterials Science and Engineering; International Union of Societies for Biomaterials Science and Engineering (1999)

Clemson Award for Contributions to the Literature, Society for Biomaterials (1997)

Fellow of Society for Advancement of Material and Process Engineering International (SAMPE) (1992)

Chapter Fellow Award, Society for Advancement of Materials and Process Engineering (SAMPE) (1990)

Engineer of the Year Award, Erie Engineering Society Council (1982)

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.
Photocopy this page or follow this format for each person.

NAME	POSITION TITLE
Steven L. Wolf, Ph.D., FAPTA	Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE (*if applicable*)	YEAR(s)	FIELD OF STUDY
Clark University, Worcester, MA	BA	1965	Biology
Boston University, Boston, MA	MS	1969	Physical Therapy
Emory University, Atlanta, GA	MS	1972	Anatomy
Emory University, Atlanta, GA	PhD	1973	Anat/Neurophysiology
Karolinska Institute, Stockholm, Sweden	Postdoctoral	1973-75	Neurophysiology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. **DO NOT EXCEED TWO PAGES.**

RESEARCH AND PROFESSIONAL EXPERIENCE

1969-70 Instructor, Anatomy and Physiology, Boston University, Boston, MA
1975-88 Principal Investigator, Emory University Rehab. Research & Training Center, Atlanta, GA
1975 Assistant Professor, Dept. of Surgery, Emory University School of Medicine, Atlanta, GA
1975-85 Assistant Professor, Dept. Anatomy, Emory University School of Medicine, Atlanta, GA
1975-78 Assistant Professor, Dept. of Rehab. Med., Emory University School of Medicine, Atlanta, GA
1978-85 Associate Professor, Dept. of Rehab. Med., Emory University School of Medicine, Atlanta, GA
1985-Present Professor, Dept. of Rehabilitation Medicine, Emory University School of Medicine, Atlanta, GA
1988-2000 Director of Research, Dept. of Rehab. Med., Emory University School of Medicine, Atlanta, GA

HONORS

Marian Williams Research Award, 1980
Georgia Merit Award, Physical Therapy Association of Georgia, 1983
Golden Pen Award, American Physical Therapy Association, 1983
Catherine Worthingham Fellow of the American Physical Therapy Association, 1987
Outstanding Research Contributor to Advancing the Understanding of Biofeedback Mechanisms, Association of Applied Psychophysiology and Biofeedback, 1987
President, Association of Applied Psychophysiology and Biofeedback, 1991-92
Helen J. Hislop Award for Outstanding Contributions to Professional Literature, American Physical Therapy Association, 1993
Award of Excellence, Section on Clinical Electrophysiology, American Physical Therapy Association, 1993
Steven J. Rose Memorial Lectureship, Washington University, St. Louis, Missouri, 1994
Lucy Blair Service Award, American Physical Therapy Association, 1996
First John V. Basmajian Lectureship, International Society of Electrophysiology and Kinesiology, 1996
Section on Geriatrics, APTA, Outstanding published paper award, 1997.
Neurology Section, APTA, Outstanding Researcher Award, 1998.

Dr. Steve Wolf Appreciation Day, February 11, 1998, Warner-Robbins, Georgia: Outstanding Contributions to Rehabilitation in Georgia.
Lester Duplechen Outstanding Faculty Teacher Award, Department of Rehabilitation Medicine, 1999.
Stroke Council, American Heart Association, 1999.
APTA Mary McMillan Lecturer, 2002

SELECTED RELEVANT PUBLICATIONS (from over 200)

Wolf SL, Catlin PA, Ellis M, et al: Assessing the Wolf motor function test as an outcome measure for research with patients post-stroke. Stroke, 2001, in print.

Sathian K, Greenspan A, Wolf SL: Doing it with mirrors - a novel approach to stroke rehabilitation. J. Neural Repair and Neuroscience,14:73-76, 2000.

Wolf SL, Catlin PA, Ellis M, Link A, Morgan B, Piacentino A: Assessing the Wolf motor function test as an outcome measure for research with patients post-stroke. Stroke, 2000, submitted for publication.

Baer HR, Wolf SL: The modified Emory Functional Ambulation Profile: An outcome measure for the rehabilitation of post-stroke gait dysfunction. Stroke, 32:973-979,2000.

Kressig RW, Wolf SL, Sattin RW, O'Grady M, Greenspan A, Curns A, Kutner M: Associations between demographic and functional characteristics to activity-related fear of falling among older adults transitioning to fraily. J Amer Geriatr Soc, 2001, in print.

Griffith, JS Kreutzer, B Pentland (eds), Rehabilitation of the Adult and Child with Traumatic Brain Injury, third edition, FA Davis, Philadelphia, 2000.

Blanton S, Wolf SL: Effectiveness of upper extremity constraint-induced movement therapy on a patient with sub-acute stroke. Physical Therapy, 79:847-853, 1999.

Wolf SL, Catlin PA, Bonner B, Marks M, Weston M: Up-training loading responses in older adults. Applied Psychophysiology and Biofeedback, 24: 179-195, 1999.

Blanton S, Porter L, Smith D, Wolf SL: Strategies to enhance mobility in traumatic brain injured patients. In M. Rosenthal, ER

Wolf SL, Gregor RJ: Exploring unique applications of kinetic analyses to movement in older adults. J. Applied Biomechanics, 15:75-83, 1999.

Blanton SR, Wolf, SL: Effects of constraint-induced movement therapy intervention on individuals with upper extremity hemiparesis. Neurology Report, 1998, 22:164.

Taub E, Wolf SL: Constraint induction techniques to facilitate upper extremity use in stroke patients. Topics in Stroke Rehabilitation, 4:38-61, 1997.

Edgerton VR, Wolf SL, Levendowski DJ: Theoretical basis for patterning EMG amplitudes to assess muscle dysfunction. Medicine and Science Sports and Exercise, 28:744-751, 1996.

Edgerton VR, Wolf SL, Levendowski DJ, Roy RR: Evaluating patterns of EMG amplitudes for trunk and neck mucles of patients and controls. International J. Rehabiltation and Health, 2:1-18,1996.

Edgerton VR, Wolf SL, Levendowski DJ: Theoretical basis for patterning EMG amplitudes to assess muscle dysfunction. Medicine and Science Sports and Exercise, 28:744-751, 1996.

Wolf SL, Segal RL, Catlin PA, Kantos H, Pate P, Raleigh T, Tschorn J: Determining consistency of elbow joint threshold angle in spastic elbow flexor muscles. Phys. Ther., 76:586-600, 1996.

Wolf SL, Segal RL: Downtraining human biceps-brachii spinal stretch reflexes. J. Neurophysiol., 75:1637-1645, 1996.

Wolf SL, Segal RL, Heter ND, Catlin PA: Contralateral and long latency effects of human biceps brachii stretch reflex conditioning. Exp. Brain Res., 107:96-102, 1995.

Wolf SL, Catlin PA, Blanton S, Edelman J, Lehrer N, Schroeder D. Overcoming limitations in elbow movement in the presence of antagonist hyperactivity. Phys. Ther., 74:35-44, 1994.

Wolf SL, Barton LA: Learned nonuse in the hemiplegic upper extremity. In Gordon WA (ed), Advances in Stroke Rehabilitation. Anover Medical Publishers: Boston, 1993, pp. 79-86.

Wolf SL, LeCraw DE, Barton LA, Jann BB: A comparison of motor copy and targeted feedback training techniques for restitution of upper extremity function among neurologic patients. Phys Ther, 69:719-735, 1989.

Wolf SL, LeCraw DE, Barton LA, Jann BB: Forced use of hemiplegic upper extremities to reverse the effect of learned non-use among chronic stroke and head injured patients. Exp Neurol, 104:125-132, 1989.

Evatt ML, Wolf SL, Segal RL: Modification of human spinal stretch reflexes: Preliminary studies. Neurosci Letters, 105:350-335, 1989.

Wolf SL, Binder-Macleod SA: EMG biofeedback applications to the hemiplegic patient: Changes in upper extremity neuromuscular and functional status. Phys Ther, 63:1393-1403, 1404-1413, 1983.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Christina M. Kwasnica M.D.	**Director of Brain Injury Rehabilitation**

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Arizona Tucson, AZ	BA	1991	Political Science
Northwestern University Medical School Chicago, IL	MD	1995	Medicine

POSITIONS:

Resident Physician Northwestern University Medical School/Rehabilitation Institute of Chicago Department of Physical Medicine and Rehabilitation Chicago, IL 1995-1999

Clinical Instructor and Cognitive Neurology Fellow Northwestern University Alzheimer's Disease Center Departments of Neurology and Physical Medicine and Rehabilitation Chicago, IL 1999-2000

Director of Brain Injury Rehabilitation Barrow Neurological Institute Phoenix AZ 2000-present

PROFESSIONAL AFFILIATIONS:

Diplomate, American Board of Physical Medicine and Rehabilitation

Fellow, American Association of Physical Medicine and Rehabilitation

Diplomate, Association of Academic Physiatrists

AWARDS AND HONORS:

Seabury Foundation Endowed Research Resident- July 1998-June 1999

NIH National Research Service Award Fellowship- F32 NS10858-01 August 1999-August 2000

Sara Baskin Award for Research Excellence- Rehabilitation Institute of Chicago- May, 1999

President's Citation- 62nd Annual Assembly of the American Academy of Physical Medicine and Rehabilitation- for outstanding paper presentation- "Predictors of Ambulation in Stroke Rehabilitation"

RESEARCH PROJECTS ONGOING OR COMPLETED DURING THE LAST THREE YEARS:

Current

Predictors of Ambulation in Stroke Rehabilitation with Dr. Richard Harvey, Rehabilitation Institute of Chicago

Pending

Unilateral Neglect and the Relationship of Measurements with Function

Prior

Bromocriptine in Unilateral Neglect- F32 NS10858-01

NIDRR Stroke Research and Training Center- Rehabilitation Institute of Chicago

PEER REVIEWED PUBLICATIONS:

Kwasnica, CM and Heinemann, A. "Coping with Traumatic Brain Injury: Representative Case Studies," Archives of Physical Medicine and Rehabilitation, April 1994, 384-389.

Grujic, Z, Mapstone, M, Gitelman, D, Weintraub, S, Johnson, N, Hays, A, Kwasnica, CM, Harvey, RL, and Mesulam, M. "Dopamine Agonists Reorient Visual Exploration Away from Neglected Hemisphere," Neurology, December 1998.

Kwasnica, CM. "Unilateral Neglect after Right Hemisphere Stroke- a Review of the Syndrome and Management," Critical Reviews in Physical Medicine and Rehabilitation, accepted for publication December, 2000.

SELECTED RECENT ABSTRACTS AND PRESENTATIONS:

Kwasnica, CM, Harvey, RL, and Mullarkey, C. "Predictors of Ambulation in Stroke Rehabilitation," Presented at the American Academy of Physical Medicine and Rehabilitation annual meeting, November, 2000

Kwasnica, CM, Cherney, L, and Harvey, RL. "Unilateral Neglect and Relationships with Functional Outcomes," Presented at the American Academy of Physical Medicine and Rehabilitation annual meeting, November, 1998.

Kwasnica, CM, Grujic, Z, Mapstone, M, and Harvey, RL. "Bromocriptine Effect on Unilateral Visual Neglect After Right Hemisphere Infarct: A Pilot Study," Presented at the American Academy of Physical Medicine and Rehabilitation annual meeting, November, 1997.

Managing Neglect Syndrome after Stroke: A Complete Experience- Annual Assembly of the American Academy of Physical Medicine and Rehabilitation, Novermber, 1998.

Managing Neglect Syndrome after Stroke: A Complete Experience- Annual Multidisciplinary Stroke Course- Rehabilitation Institute of Chicago, April 1999

Pharmacology of Brain Injury- Rehabilitation Institute of Chicago- December 2000

Non-traumatic Brain Injury- Rehabilitation Institute of Chicago- December 2000

Pharmacologic Approaches to Motor Recovery after Stroke- Annual Multidisciplinary Stroke Course- Rehabilitation Institute of Chicago- April 2000

Atypical Dementias- Grand Rounds- Ingalls Hospital- Chicago, IL- April 2000

Neuroplasticity and Rehabilitation- Grand Rounds- Rehabilitation Institute of Chicago- July 2000

EXHIBIT B

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Douglas E. Wendelboe	Software Consultant; President, Penn Microsystems

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Pennsylvania State University, State College, PA	BS	1972	Electrical Engineering
University of Pennsylvania, Philadelphia, PA	MS	1976	Electrical Engineering

RESEARCH AND PROFESSIONAL EXPERIENCE

1998-Present Software Consultant, BTI Consultants, Tempe, AZ. Design of hardware and software for medical devices

1981-Present President, Penn Microsystems. Consulting on microprocessor-based products. Medical device projects include:

- Hand-held Blood Prothrombin-Time Measuring Device, San Jose, CA, 2000-Present
- Designed and implemented the Automated Calibration and Test System for the Bone Growth Stimulator, Phoenix, AZ, 1999-2000
- Firmware enhancements for an electromagnetic Bone Growth Stimulator, Phoenix, AZ, 1997-1999
- Developed an Automated Active Burn-In System for the Bone Growth Stimulator, Phoenix, AZ, 1996-1997
- Designed and implemented firmware for Nerve Integrity Monitor Instrument, Jacksonville, FL, 1994-1995
- Designed, implemented, and maintained the firmware for a line of Micro-titer Plate Readers, Winooski, VT, 1982-1985
- Designed and implemented the complete firmware for a Pacemaker Systems Analyzer, Winooski, VT, 1980-1981

1977-1981 Senior Associate Engineer, IBM Corp., Essex Junction, VT

1976-1977 Senior Product Engineer, Honeywell Corp., Ft. Washington, PA

1972-1976 Design Verification Software Engineer, UNISYS (Sperry-Univac), Blue Bell, PA

PROFESSIONAL PUBLICATIONS

"Recommended Use of the PL/M Computer Language in Safety-Related Systems," Report for the Nuclear Regulatory Commission, NUREG/CR-6463, June 1996

Co-publisher of the Annual "Arizona High Tech Directory"

Columnist for the "Arizona High Tech Times" newspaper

PROFESSIONAL

IEEE Computers, IEEE Software, IEEE Management, IEEE Biomedical

American Society for Quality

TECHNICAL SKILLS

Languages: Keil C51 w/uVision2, IAR C, PIC-C, 8051, 8x86, 68xx, 68xxx assembler, Microchip PIC, Hitachi H8 assembler, TMS320C54x Algebraic assembler, National Instruments LabWindows/CVI, Microsoft Visual C++, Visual Basic

RTOS: uC/OS-II, QNX, Keil RTX-51, familiarity with VxWorks, Tornado

Microprocessors: Intel 8051, 80251, 8X93x USB, Intel 80x86, 80188, 386EX, 68HC05, 68HC08, 68HC11, 68xxx family, Hitachi 6303, H8S/2134, Microchip PIC16C74, 16C65, ST Micro ST10F167/168

In-Circuit Emulation: Intel ICE 8051, 8085, 80188, 80x86, Nohau EMUL51-PC: 80C552, 89C51RD2, Microchip PIC-Master & others

Peripheral Buses: I^2C, CAN v2.0, USB, Motorola SPI, Dallas Semiconductor interfaces

Design Standards: IS)-9001 Design Quality Standards, FDA (97-4179) Medical Device Quality Systems Standards, FDA 510(k), FDA Pre-Market Approval (PMA)

Bus Boards: PC/104 Bus, STD Bus, VME Bus

Logic: SPICE Simulation, Programmable Logic Compilers

Network: TCP/IP, WATTCP

Database: MS SQL7, Oracle, Informix

EXHIBIT B

Koeneman, James Bryant

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Edward J. Koeneman	Consultant

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Arizona State University, Tempe, AZ	BSEET	1992	Electronic Engineering
Arizona State University, Tempe, AZ	MT	1994	Electronic Engineering

POSITIONS

1999-Present	BTI Consultants, Consultant.
1997-1999	Adtron Corp., Mesa, Arizona. Product Manager, Data Storage Devices.
1997	PCI Medical, Phoenix, Arizona. Design Engineer, Medical Electronics.
1995-1997	Prescom Electronics, Mesa, Arizona. Chief Engineer, Contract Electronic Design and Manufacturing.
1988-1995	Harrington Arthritis Research Center, Phoenix, Arizona. Lab Coordinator for Orthopaedic Resident Projects, Mechanical Testing.

PEER REVIEWED PUBLICATIONS

Koeneman, E.J., J.A. Lerman, R.J. Haynes, J.B. Koeneman, W. B. Wong, "A Biomechanical Comparison of Gardner-Wells Tongs and Halo Device Used for Cervical Spine Traction," SPINE, Volume 19, Number 21, pp. 2403-2406, 1994.

Koeneman, E.J., N.R. Crawford, A.G.U. Brantley, C.A. Dickman, "An Apparatus Applying Pure Nonconstraining Moments To Spine Segments In Vitro," SPINE, Volume 20, Number 19, pp. 2097-2100, 1995.

SELECTED PRESENTATIONS

Koeneman, E.J., J.A. Lerman, J.E. Maisel, J.B. Koeneman, "Electromyographic Analysis of the Hockey Slapshot," Presented at 1994 Fall Meeting of the Biomedical Engineering Society.

AWARDS AND HONORS

IEEE Outstanding Student Achievement Award, 1993

EXHIBIT B

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Donald E. Herring	Senior Industrial Design Consultant

EDUCATION (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
American University, Washington, DC	BA	1967	Govt. and Public Admin.
Arizona State University, Tempe, AZ	BS	1982	Product Design
Arizona State University, Tempe, AZ	MSD	1993	Human Factors and Design

PROFESSIONAL EXPERIENCE

2001-Present	Senior Industrial Design Consultant, BTI Consultants, Tempe, Arizona
1998-Present	Assistant Professor, Arizona State University, Tempe, Arizona
1997-1999	Proprietor, Redfish Design, Phoenix, Arizona
1994-1997	Assistant Professor, Purdue University, West Lafayette, Indiana
1992-1994	Exhibit and Industrial Designer, Sunbelt Scenic Studios, Inc., Tempe, Arizona
1991-1992	Exhibit Designer, Giltspur Exhibits, Phoenix, Arizona
1982-1989	Senior Project Designer, Mattel Toys, Hawthorne, California
1975	Arizona Real Estate Sales and Brokerage, Phoenix, Arizona
1973	Specialist, United States Treasury Department, Washington, D.C.
1972	Foreman, Athens Paint & Drywall Company, Alexandria, Virginia
1968	OJT Contract Writer, Washington Urban League, Washington, D.C.
1968	Capitol Policeman, United States Capitol Building, Washington, D.C.

PRINCIPAL PROFESSIONAL PUBLICATIONS AND PRESENTATIONS

"Children's Computer Human Factors and Seating Recommendations" (For Our Greatest Future Resource), Natural Resources, 1995 IDSA Design Education Conference Proceedings, Santa Fe, New Mexico, September 1995

"Twenty Years Later: What Are the 11982 Graduates of an Industrial Design Program Doing in the New Millennium?," Gumbo, 2000 IDSA Design Education Conference Proceedings, New Orleans, Louisiana, September 2000

MEMBERSHIPS IN SCIENTIFIC AND PROFESSIONAL SOCIETIES

Human Factors and Ergonomics Society of America
Arizona Chapter Member of the Human Factors and Ergonomics Society of America
Industrial Design Society of America (IDSA)
The Arizona IDSA Chapter Secretary (Founding member and officer)
The Indiana IDSA Chapter Secretary/Treasurer (Resigned, April, 1997)

PATENTS

U.S. Patent 4,787,876 - Toy Musical Play Set, 11/29/88, assigned
U.S. Patent 4,673,373 - Transformable Toy Block, 6/16/87, assigned
U.S. Patent 4,645,471 - Busy Ball Child's Toy, 3/7/85, assigned

AWARDS, SCHOLARSHIPS AND HONOR SOCIETIES

Netherlands Toy of the Year Award to Disney Pots and Pans Band based on Originality, Safety and Suitability, 1988

Second Place Award ($2,000.00) in Mattel's Toy of the Year Contest for the Invention and Development of the Double Dooz Transformers Toy Line, 1986

Nominated for the Mattel Toys Presidents Award for Leading a "Brainstorming Event" with 40 Participants Producing 100 Product Concepts for Presentation in Ten Days, 1985

Mattel $2000.00 Discretionary Award for "The First Innovative Preschool Product Line to Come out of Mattel in Eight Years," 1985

Arizona State University Outstanding Senior Industrial Design, 1982

Honorable Mention ($250.00) in Mattel Toy Design Contest, 1982

Awarded Internship at Mattel Toys, 1982

Phi Kappa Phi National Honor Society, 1982

• Principal Investigator/Program Director (Last, first, middle): Koeneman, James Bryant

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Cristobal Neal Eblen, Ph.D.	Director of Planning, Research and Program Evaluation

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Marist College	BA	1976	Psychology
Marist College	MA	1978	Community Psychology
Arizona State University	Ph.D.	1987	Social Psychology

NOTE: The Biographical Sketch may not exceed four pages. Items A and B may not exceed two of the four-page limit.

A. **Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

Post-doctoral Research Fellow (Harrington Arthritis Research Center) 1987-89
Psychologist I (AZ Department of Corrections) 1989-90
Psychologist II (Arizona State Hospital) 1990-91
Research and Statistical Analyst III (AZ Division of Behavioral Health Services) 1991-93
Psychologist II (Southern Arizona Mental Health Center) 1993-96
Psychologist II (AZ Department of Corrections) 1996-97
Research Associate (Community Partnership of Southern Arizona) 1997-2000

B. **Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation.

Eblen, C. & Koeneman, J. (1993). A longitudinal evaluation of a four-wheeled walker: Effects of experience. Topics in Geriatric Rehabilitation, 8, 65-72.

Eblen, C. (1992). Evaluation of assistive devices. Topics in Geriatric Rehabilitation, 8, 6-11.

Eblen, C. & Koeneman, J. (1991). A multi-dimensional evaluation of a four-wheeled walker. Assistive Technology, 3, 32-37.

C. **Research Support.** List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and responsibilities of principal investigator identified above.

N/A

RESOURCES

FACILITIES: Specify the facilities to be used for the conduct of the proposed research. Indicate the performance sites and describe capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Under "Other," identify support services such as machine shop, electronics shop, and specify the extent to which they will be available to the project. Use continuation pages if necessary.

Laboratory:

KMI leases 1,433 square feet of office and laboratory space. Our lab contains the latest in hardware support tools such as: Logic analyzers, analog & digital oscilloscopes; I2C, USB and CAN bus analyzers; Internet server with TCP/IP tools. We also maintain the latest in software compilers, assemblers, simulators, and other software development tools for microprocessors and systems.

We have a complete model shop for the development of prototypes. This includes saws, sanders drill press and a complete supply of hand tools. We have a complete drafting facility.

These facilities are dedicated to the development of the device described in this proposal and to extensions of the design.

Clinical:

All clinical evaluations will be done at the Barrow Neurological Institute (BNI) of St. Joseph's Hospital in central Phoenix. It was first accredited by the Commission on Accreditation of Rehabilitation Facilities (CARF) in 1988. BNI has a state-of-the-art rehabilitation facility and participates in many clinical rehabilitation research studies. Space and equipment for the clinical evaluations will be available for this study.

Animal:

NA

Computer:

Various computer simulation programs such as AutoCAD, Photoshop, Illustrator, Humanoid, Perception Video Capture Hunamoid run on eight Pentium computers.

Office:

The office has complete facsimile, copying and printing facilities.

Other:

The KMI facility is adjacent to BTI Consultants that provides secretarial and technician support and miscellaneous consulting on an as needed basis.

MAJOR EQUIPMENT: List the most important equipment items already available for this project, noting the location and pertinent capabilities of each.

See above.

INTRODUCTION

BTI Consultants submitted the original proposal. Because of clinical interest in this device, a separate company, Kinetic Muscles, Inc. (KMI) was formed in May 2001 and is now submitting this proposal. The PI and most of the participants are unchanged from the original proposal. Steven Wolf, Ph.D., PT, FAPTA, who is a clinician specializing in stroke rehabilitation and a well-respected research scientist in motor control is now a consultant. The scope of work for the original proposal involved fully developing the device per design control procedures. The work of Phase I has essentially been completed. Therefore, the Experimental Design has been completely rewritten to be a pilot clinical study, and because of this extensive rewrite, content changes are not indicated by change in font. The comments that follow are in sequential response to the concerns expressed by the reviewers on the summary statement of the original grant proposal. Their concerns are summarized, followed by our response. The responses are first **lettered** and **the narrative page number** where the total response can be found is given next.

Reviewer 1:

A. (pages 19-22) **Need for more detail on the design.** An overall block diagram of function is included and a more complete description included.

B. (pages 19,22,23,27) **What are the training parameters? How are issues of spasticity, ADLs, fatigue, etc. addressed**? A more thorough description of the treatment protocol is included in this revision and the resistance due to wrist and finger flexor spasticity is measured and fed back to the patient. The safety features of the patient being able to stop and start treatment at any time, the panic button, limit on force and range of motion are described in this revision. Activities of Daily Living (ADLs) are encouraged when the device is not being used.

C. (pages 19,24) **How will compliance be monitored? What about issues of durability, maintenance and robustness of the device?** The design description includes how compliance is recorded by the microprocessor. Maintenance and reliability will be evaluated by recording patient calls for assistance and by the final patient questionnaire.

D. (pages 19,27) **Define safety features.** The safety features are described in more detail.

E. (pages 23-25) **Define the evaluation procedure elements and when and how they are evaluated. How do project/development goals relate to ultimate feasibility?** To address the issue of feasibility, standard patient performance tests are included as is the determination of feasibility based on quantifiable improvements in function and patient compliance with the therapy protocol

F. (pages 6-8,13,23-26) **There is a need to relate design implementation and value to investigators background.** More detail on the protocol is included and the biodata sheets of Drs. Wolf and Eblen are added.

G. (pages 6-9,26,27) **There is a need for detail about subject/user characteristics.** In addition to the physiatrist, Dr. Kwasnica, we have added Dr. Wolf, an experience physical therapy researcher as a consultant, and Deborah Taylor, the physical therapist that will make all functional measurement. All of these clinicians have experience working with patients described in study entrance criteria.

H. (pages 6-9,23,24) **Lack of awareness between what the device will do and movement characteristics achieved.** Dr. Wolf has agreed to be an active consultant and correlations of physiological changes with functional changes included.

I. (pages 26,27) **Gender, minority or children issues must be discussed in great detail.** The patients expected to participate in the study are representative of those seen by physicians in this area.

Reviewer 2:

A. (pages19,20,22) **The device appears unwieldy.** The fully developed design described in this proposal has a battery driven micro-compressor that is very quiet and is lightweight. The patient perception of the unwieldiness will be evaluated in the Patient Acceptance Questionnaire. There is elastic recovery inherent in the driver.

B. The evidence for utility of Functional Electrical Stimulation is questioned. We agree that there are minimal results reported in the literature supporting the effectiveness of this treatment. To better evaluate the effectiveness of this treatment we have removed the neurostimulation component from the device in this study and will study it separately.

C. (pages 19,21,22) **More detail is needed for the EMG biofeedback function.** Diagrams of and descriptions of electrode placement and use in informing the patient of wrist extensor activity is described.

D. Same as Comment E from reviewer 1.

E. What is meant by massed practice? As discussed in the referenced literature, "massed practice" refers to repetitive practice in using the limb for many hours a day for a period of consecutive days.

F. Same as Comments D. and I. from reviewer 1.

Reviewer 3: This reviewer brought up the issues of lack of detail, feasibility assessment and more clinician involvement. These have all been discussed with respect to the other reviewers comments

A. SPECIFIC AIMS

The **primary purpose** of this project is to improve the restoration of physical function of stroke patients by incorporating into one device, the treatment modalities of massed practice therapy, and force and electromyographic (EMG) biofeedback. Each of these approaches may in and of itself demonstrate varying degrees of success in treating stroke patients. The device will assist therapy by supplying increased amounts of information to the physician and therapist while reducing the amount of patient contact time. The device will be adaptable to accommodate the changing paradigm of CVA rehabilitation service delivery and to assist in studies designed to refine therapy protocols. The **hypothesis** to be tested is whether it is feasible for this biofeedback device to improve stroke patient physiological and functional performance. Using the wrist joint as a model, this approach will be deemed feasible if there is an increase in active range of wrist motion of 10% per week and there is a positive correlation between active wrist motion changes and changes in functional improvement as measured in the Wolf Motor Function Test (WMFT).

The **specific aims** of this proposal are:

1. Determine patient compliance to an extensive practice, at-home therapy protocol.
2. Measure the patient physiological changes of active range of wrist extension, EMG extensor activity, and flexor force resistance to motion during the course of therapy.
3. Ascertain patient functional changes over the course of therapy.
4. Analyze the relationship between functional changes and physiological changes.

B. BACKGROUND AND SIGNIFICANCE

Many people have movement disabilities caused by disease or injury. Among the causes are cerebrovascular accident or stroke (CVA), traumatic brain injury, multiple sclerosis, spinal cord injury and Parkinson's disease. This project focuses on stroke; however the results will have application to other causes of movement disability. Stroke is the leading cause of disability in the United States with at least 700,000 new cases each year [1-3]. Over half of these people have residual physical disability. Current stroke therapy is labor-intensive and costly. Often insurance does not cover the cost of full therapy. One estimate is that the United States spends $30 billion per year to take care of stroke survivors. Seventeen billion dollars of this cost is direct medical expenditures and thirteen billion dollars represent an indirect cost due to lost productivity [3]. Another estimate is that the total direct and indirect costs of stroke are $43.3 billion per year [3]. The number of strokes is projected to increase because of the increase in the over 50 "baby boom" population. Also, new pharmaceutical treatments for stroke are projected to increase the number of patients surviving a stroke and increase the percentage of stroke survivors requiring rehabilitation. Therefore, it is not surprising that a recent estimate indicates the prevalence of stroke will more than double over the next 50 years [2].

Because of health care reimbursement reductions, therapy time for stroke patients has been significantly decreased. Currently, a majority of time spent in therapy post-stroke concentrates on helping a patient adapt to their disability by teaching toileting skills and transfers. A consequence of this treatment is the emergence of "learned nonuse" that hinders the restoration of available function [2]. Most current rehabilitation therapies are administered on a spaced basis. Recently, concentrated therapies have been developed that improve function in CVA patients by reversing the effects of "learned nonuse"[4]. Animal studies suggest that learned nonuse is established immediately after the initial organic damage. A patient is punished for trying to use the affected limb and is rewarded for using other parts of the body. Over time, healing of the

organic damage occurs but the suppression of use learned in the acute phase remains in force [4]. As discussed by Taub [4], many of the therapies that have been shown to be effective in restoring function involve massed practice. Physical Therapy training techniques were used by Bach-y-Rita [5,6] and Franz, Scheetz, and Wilson [7]. Significant improvement in limb function was obtained in chronic CVA patients. Training techniques based on EMG biofeedback improved motor ability of chronic CVA patients, as demonstrated in studies by Wolf [8,9], Basmajian [10, 11], and Balliet [12]. Repetitive concentrated practice produced large therapeutic effects for lower limb function [13, 14, 15]. Taub (2,32) has systematically studied a variation of forced use of hemiplegic extremities, originally described by Wolf (31,35,36). Taub has labeled this therapy Constraint-Induced (CI) Movement Therapy [2, 32]. His group has shown positive results in controlled randomized studies [16]. Some of these experiments compared several massed therapy techniques and all showed very large increases in limb use over the treatment period.

Two very sophisticated robot systems are being developed for treatment and evaluation of CVA patients [1, 17]. These devices have shown some effectiveness in treatment of CVA patients and have developed very useful data for understanding recovery mechanisms; however, the current cost of these systems precludes their widespread clinical use [18].

Other studies show that measured EMG can be used to trigger neuromuscular electrical stimulation in restoring function to CVA patients [26, 27, 28, 29]. However, the discomfort of surface neuromuscular stimulation significantly limits the clinical implementation of this modality for persons with hemiplegia [34]. EMG biofeedback treatment of stroke patients has also shown some success [30, 31, 12, 8]. This treatment uses surface electrodes to capture the electrical activity of a selected muscle group. An electronic unit converts the signals into visual or audio information for the patient. This information is used by the patient to augment or decrease muscle activity.

A device that has a venerable history in supplying motion to assistive devices is the pneumatic artificial muscle. The artificial muscle exhibits many of the properties of human muscle. The device consists of an expandable internal bladder, e.g., a rubber tube, surrounded by a braided shell. When the internal bladder is pressurized, it expands radially against the braided shell. The pressure on the inside of the braid causes it to contract. Braided finger traps used to hold fingers on traction devices contract radially when pulled. The **air muscle** works in the same manner only in the opposite direction, i.e., increasing the diameter causes it to shorten. Like human muscle, the device has spring-like characteristics, is flexible, and is lightweight. The force-deflection characteristics can be made similar to those of human muscle. This type of device was first used in the 1950's for powered braces [19, 20]. Pressurized air canisters or accumulators that are recharged by air compressors supply air. Major advantages of the air muscle are its flexibility and ease of adaptation to address the specific loss of function exhibited by a patient. This type of device is often referred to as the McKibben Artificial Muscle. The device has three times the pull force of an air piston of the same cross sectional area. **The potential utility of this device resides in its unique combination of attributes: low cost, light-weight, low profile, and low noise operation.** The device has not been used extensively, because it has been applied in the wrong applications and has suffered from the lack of engineering in critical areas. Research on the application of the air muscle has been revived by the University of Washington [21, 22, 23, 24, 25]. The Shadow Organization in England uses the air muscle to operate biped and multiped robots [33].

C. PRELIMINARY STUDIES

The labor-intensive and long treatment times of forced practice make effective rehabilitation expensive. A promising approach to providing a lightweight, low-cost stroke therapy device is a system that synergistically combines four modes of feedback that individually have been shown to be effective (visual

presentation of desired motion, resistive-force of wrist flexor muscles and EMG activity of the extensor muscles). We have constructed a prototype of an air muscle powered therapy device for the hand and wrist that has the adaptability to be used in current treatment modalities and also in the refinement of rehabilitation methods. Figure 1 is a drawing of the device. An air muscle is attached to the proximal forearm. Activation of the air muscle rotates a bar that extends the wrist and operates a four-bar mechanism that extends the fingers. Wrist extension position is measured by a potentiometer that is incorporated in the device pivot. Resistance to extension is measured by force sensitive resistors (FSRs) placed on the driving bar. This is a measure of the combined wrist and finger flexor muscle resistance. Surface electrodes measure wrist extensor EMG activity. The location of the EMG electrodes is determined for each patient by the therapist. Figure 2 shows the method of permanently attaching the electrodes to the device. The method locates the electrodes on the same place on the patients arm for each therapy session. Air to activate the muscle is supplied by a microcompressor powered by a rechargeable 12-volt battery. A microprocessor controls the activation of the air muscle by operating the microcompressor and a 3-way valve. Wrist position is displayed as a bar graph on the LCD. The changing goal for active wrist motion is displayed as a line on the graph. One line of multi-color light emitting diodes (LEDs) indicates the degree of flexor resistance torque as measured by the force sensitive resistors. A second line of LEDs indicates the EMG activity of the wrist extensors. The microcompressor, battery, 3-way valve, microprocessor, and the LCD are in a plastic box that sits on a table during therapy sessions. The LEDs are arranged in lines on the plastic support structure on the arm. A coiled cable assembly that contains the electrical wires and air hose connects the box to the activation device. The batteries have the capacity to provide six hours of therapy a day and are recharged overnight. This system is a self-contained, mobile device that provides visual feedback of wrist and hand position, EMG wrist extensor activity and combined wrist and finger flexor resistive torque. The firmware in the microprocessor has been designed to be well-structured using object-oriented programming techniques. Use of these techniques yields more reliable code having fewer discrepancies and problems. Each of the object components was tested separately (component testing). When the firmware was integrated with the electronic hardware, the complete system was tested (system integration testing). Finally, the operation of the complete device was validated and verified for function by comparing to the design requirements established at the project beginning. The essence of the design requirements is described in this proposal. A block diagram of the system is shown in Figure 3. The real-time clock/calendar is powered by a battery mounted on the printed circuit board when the power is off. The clock maintains the time and date continuously. Records of patient use, active range of motion, extensor resistive torque, and EMG activity are recorded with a time stamp in a non-volatile serial EEPROM memory device. Data is kept safe, even when no power is applied to the memory. These records can be downloaded to a Windows application on the therapist's personal computer. The results are sorted by patient and tabular and graphical displays made available for viewing.

D. EXPERIMENTAL DESIGN AND METHODS

A pilot study will be conducted to determine the feasibility of this device to improve stroke patient physiological and functional performance.

Patient Population – The patient entrance criteria will be similar to the Extremity Constraint-Induced Training Evaluation (EXCITE) trial [37] except that patients must be more than 3 months post stroke with no limitation on the maximum time since their stroke. Patients must be at least 18 years old. A patient must be able to actively obtain more than 10° of wrist extension plus 10° of the thumb and at least two fingers 3 times in one minute. The patient must be able to independently and safely transfer to the toilet, stand-up and maintain balance for 2 minutes with arm support.

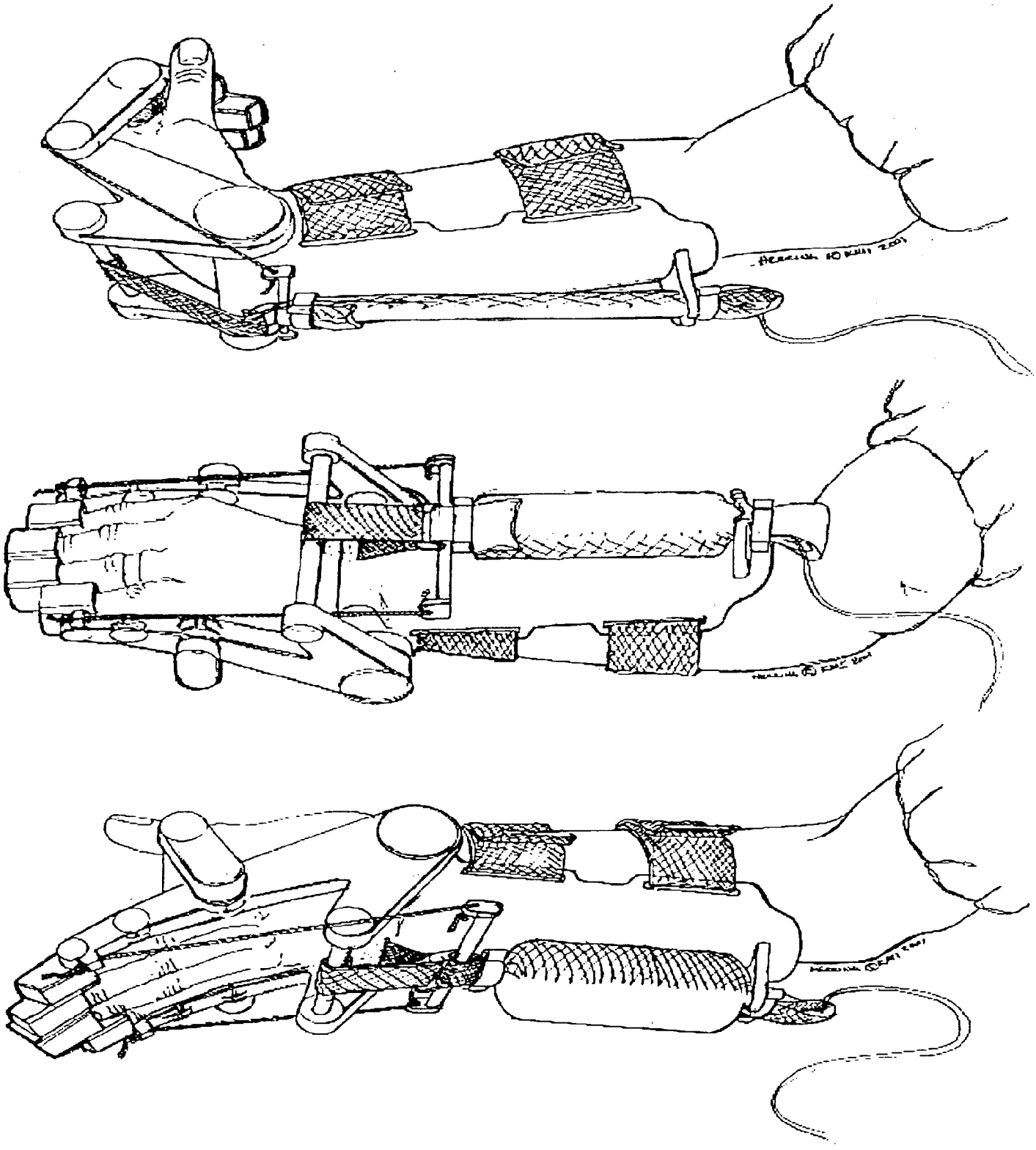


Figure 1 Therapy Device in Flexion, Neutral and Extension, Shrouding, LEDs and Control Box not shown for Clarity

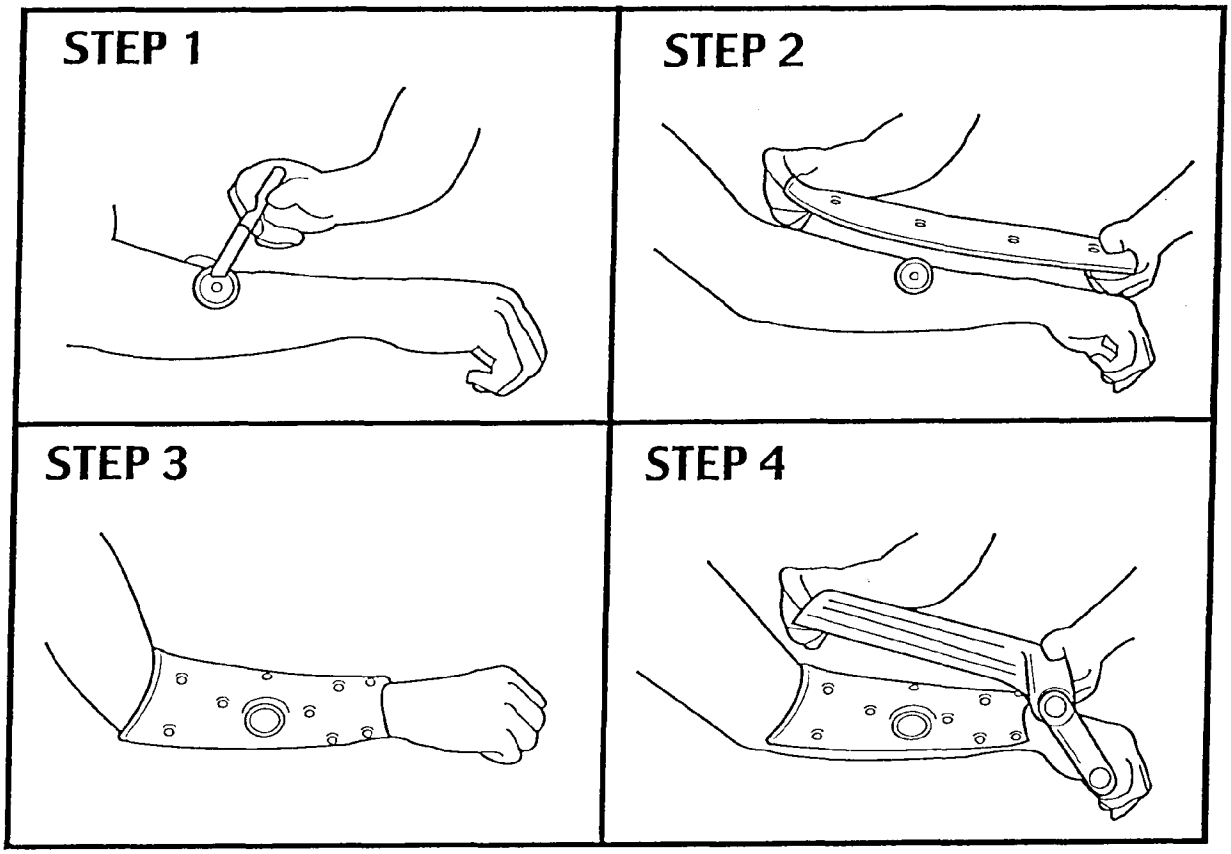


Figure 2 Attachment of EMG Electrodes.

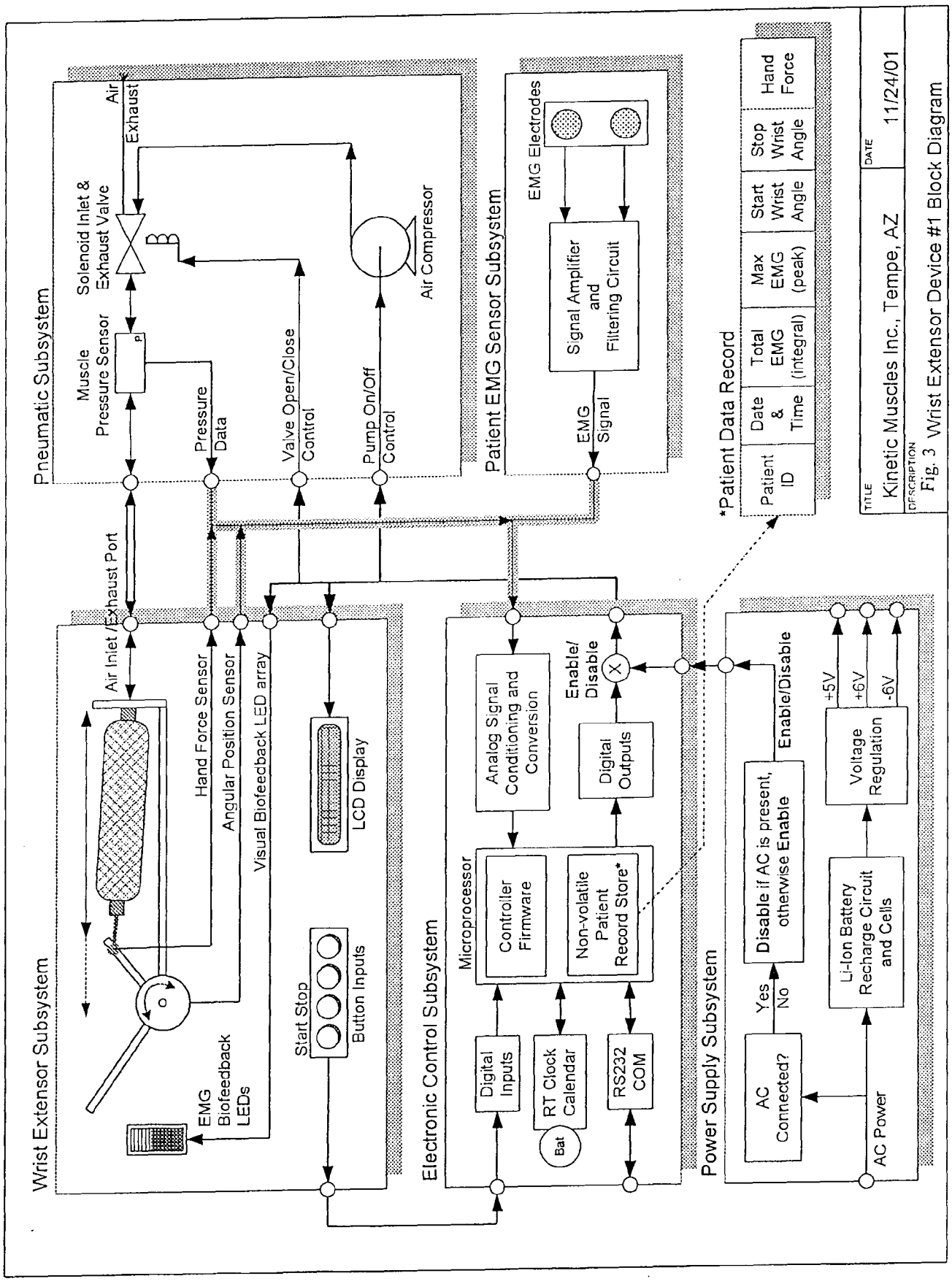
Step 1: Therapist places electrodes so they measure wrist extensor activity. Transferable mark is placed on electrode.

Step 2: Carrier fabric is placed on arm. Hole is punched out for electrode.

Step 3: Carrier draped over arm around electrode.

Step 4: Plastic shell of device is placed over carrier and electrode. Adhesive on underside of shell adheres to carrier. Electrode is now part of shell and electrode is indexed with respect to palmar each time patient applies device.

EXHIBIT B


Pneumatic Subsystem
Air
Exhaust
Solenoid Inlet & Exhaust Valve
Muscle Pressure Sensor
Pressure Data
Valve Open/Close Control
Pump On/Off Control
Air Compressor
Patient EMG Sensor Subsystem
EMG Electrodes
Signal Amplifier and Filtering Circuit
EMG Signal
*Patient Data Record
Patient ID
Date & Time
Total EMG (integral)
Max EMG (peak)
Start Wrist Angle
Stop Wrist Angle
Hand Force
TITLE
Kinetic Muscles Inc., Tempe, AZ
DATE
11/24/01
DESCRIPTION
Fig. 3 Wrist Extensor Device #1 Block Diagram
Exhaust Port
Air Inlet /
Wrist Extensor Subsystem
Hand Force Sensor
Angular Position Sensor
Visual Biofeedback LED array
LCD Display
Start Stop
Button Inputs
EMG Biofeedback LEDs
Electronic Control Subsystem
Microprocessor
Controller Firmware
Non-volatile Patient Record Store*
Analog Signal Conditioning and Conversion
Digital Outputs
Enable/ Disable
Digital Inputs
RT Clock Calendar
Bat
RS232 COM
Power Supply Subsystem
AC Connected?
Yes
No
Disable if AC is present, otherwise Enable
Enable/Disable
Li-Ion Battery Recharge Circuit and Cells
Voltage Regulation
+5V
+6V
-6V
AC Power

Patients are excluded from the study if they have had more than one stroke, have excessive cognitive impairments, lack of stamina, pain in the impaired extremity or serious, uncontrolled medical conditions.

The goal is for 15 patients complete the study. Because dropout rates of 10% to 24% have been reported in rehabilitation trials, we will recruit 25 patients. The three physicians involved with this study have already identified that many potential participants from their past or present patients.

Evaluation – Our physician colleagues will select patients whose medical records indicate that they meet the entrance criteria. The patients will be called into the clinic for an initial evaluation. After demonstrating and documenting that they meet the minimum requirements the patients will be asked to enter into a Behavioral Contract that expresses the investigators expectation that they comply with the protocol, that their participation is very important to improving therapy for stroke patients, and that the investigators are obligated to be responsive to questions and be available to the patients at reasonable times. The patient will be asked to sign the patient consent form.

Deborah Taylor, a registered occupational therapist who specializes in conducting clinical studies, will administer therapy. A patient history of age, type of stroke, date of stroke and previous treatments will be recorded. The therapist will document baseline patient wrist and hand performance as soon as the patient enters the study. The degree of true grasp reflex in response to palmar skin surface stimulation will be measured and recorded. The Wolf Motor Function Test (WMFT) [38] and the Frenchay Arm test [37] that have been validated in the literature will be used to assess function [**Specific Aim 3**]. The therapist will explain the operation and purpose of the device. A brochure describing the device and contact information will be provided the patient. The therapist will then place the EMG electrodes on the patient and attach them to the device. The therapist will demonstrate several treatments of the device. The device will be removed and the patient asked to attach the device and start treating without any help. The patient will be given a diary to record activities that he/she perform to attempt to manipulate the environment by the affected limb during the two weeks of the study. The patient will be instructed to attempt activities that they haven't done yet as function improves. The patient will be required to return after one week and at the end of two weeks for repeat functional evaluations. At the end of the study, the patient will be asked to fill out a questionnaire rating on an ordinal scale their impression of the device weight and bulkiness, their fatigue during therapy, the effectiveness of the LED and LCD feedback methods, the reliability of the device and they will be asked to provide suggestions.

Protocol – The patient is instructed to try to extend the wrist and fingers when a beep is heard. The EMG activity of the wrist extensors and the motion of the wrist [**Specific Aim 2**] are recorded in the memory of the device and displayed for the patient. The patient will be instructed to use the device for at least 6 hours a day, although more treatment is allowed. The treatments do not have to be continuous. The patient can start and stop the device at any time. The first 2 hours will emphasize EMG and joint position feedback. During the second 2 hours the flexor resistance torque from the flexors will be used as the feedback signal to help the patient reduce any flexor spasticity. The final 2 hours of therapy will have both extensor EMG and flexor resistance torque as feedback. The number of completed cycles will be recorded for each day as well as the time for each cycle and the total treatment time for each day. A 2 inch by 4 inch by 4 inch block is provided the patient. The patient is encouraged to grasp the block and lift it several times during a day and at the end of each therapy session. After grasping the patient is encouraged to try and lift and move the block. The patient is encouraged to keep a record of successful attempts.

The level of extensor EMG activity is indicated by LEDs. A level equal to that obtained at the last clinic therapy session shows a yellow light. A level below that level generates a buzzing sound. A green LED will indicate a higher level. Faster flashing LEDs will indicate higher levels of EMG activity. The output of the

joint position sensor is displayed on the LCD by a bar. If motion exceeds this line a pleasant sound is heard. After every day, the line that represents the goal is increased by 1% of the highest joint motion achieved in the previous day. Thus joint position serves as the basis for subsequent training each day.

During training, whenever motion has stopped for 3 seconds, the air muscle is activated and the wrist and finger extension is completed. The extension is held for 3 seconds and then released. The torque of the wrist and finger flexor resistance is measured and displayed on flashing red LEDs during the process. The higher the force, the faster the blinking. The patient will be instructed to try to minimize this force by thinking about relaxing the flexors. There is then a system delay of 10 seconds and the process started over with a beep.

The number of hours of operation of the device and the active motion achieved at the beginning of a day and at the end of each day is recorded in memory [**Specific Aim 1**]. This information will provide us with accurate information about patient compliance and allows us to match up our timed data from patient reports of self-documentation of training. When the device is turned on for the first time each day, these parameters are displayed for the patient on the LCD.

The memory of the device will be downloaded onto a PC in the clinic. A summary chart graphically displaying the number of hours of use a day by the patient, the range of motion change per day and the change of active range of motion day to day will be displayed and the charts printed for the patient file.

Data Analysis -
Measures: There are four types of data collected in this study:

(1) The *number of hours* of use per day by the patient. This is a measure of *compliance* with treatment and will be used to assess both functional improvements and study termination (i.e., dropout rate).

(2) The *physiological parameters* of wrist extensor EMG, wrist and finger flexor resistance torque, and active range of motion. *Range of motion* will be examined as a dependent variable, while resistance torque will be examined as both a dependent measure and a possible moderator factor influencing compliance and dropout rate.

(3) *Functional changes* in hand and wrist function are measured by standard test protocols at baseline, one week and at the end of the study. Attention will be made to assess those *functional assessments* in the protocol that should directly be impacted by this treatment; other assessments will be examined for generalization of functional improvement.

(4) *Patient activities and acceptance* of the device are recorded in self-report questionnaires. It is expected that self-reported acceptance and increase in activities will be related to compliance, physiological and functional gains.

Design and Statistics. The basic comparison is baseline with two time measurements (one week and post treatment). Specifically, physiological and functional changes will be examined using pre-post statistics. A Friedman test for repeated measures will be used to determine significant changes from baseline and post-test periods (baseline-one week comparisons will also be examined). To determine precise areas of change, follow-up Wilcoxon rank tests will be employed on individual measures.

Of specific interest will be the physiological range of motion assessment and those functional measures that are related to wrist functioning. This will help in reducing the multiple comparisons. The resistance torque will also be examined in this manner; however, correlational analyses will also be conducted to assess possible effects of spacticity as a moderator of success. Graphs plotting this relationship will be used to assess possible curvilinearity. **[Specific Aim 4]**

Given the small N in this study, there may be problems with the amount or quality of change variation to detect degree of improvement with initial disability. This analysis will be conducted. Correlation coefficients will be calculated between the physiological response changes (i.e., grasp reflex) and functional changes as well as reported changes in activities and compliance.

Finally, patient acceptance of the device and suggested improvements will be entered into the design control system for the device for evaluation. Correlations will be calculated between reported compliance and actual hours of use.

The device will be considered acceptable and feasible if patient compliance is sufficient to result in statistically valid improvements in both physiological function and functional measures. **[Hypothesis Test]**

Limitations - By taking patients as early as 3 months post stroke, there may be some spontaneous recovery; however, it coincides with the lower limit of the EXCITE study. Also, Duncan has shown that the most dramatic motor recovery occurs in the firs 30 days following a stroke for all degrees of stroke severity [39]. We do not know if we are bringing sub-acute patients back to a pre-existing level or making absolute improvements. However, the study does measure the feasibility of usage and functional improvement. Because of the six-month limitation of a Phase I grant, follow-up to examine retention of gains or potential increased improvements with more therapy cannot be made. While the numbers of minority and ethnic people in this study preclude statistically significant comparisons, the main purposes of this study are to refine the protocol for a larger Phase II study and to investigate feasibility of this therapeutic device in a group of patients.

Design Issues – The sensitivity of the EMG measurement to forearm motion and relative motion of muscles with respect to skin will be examined. The repeatability of placement of the electrodes from use to use will also be evaluated. Skin sensitivity to the pressure of the device or type of material will be examined.

Project Plan - Table I is a time line (Gantt chart) of the Phase I tasks. Since six months is a brief time to conduct a pilot study, 90 days before the award of the study we will request NIH approval to accumulate costs before the beginning of the grant period. The early tasks would allow the patient portion of the study to begin immediately at the time of award. After NIH approval of early cost accumulation, the first task is to have an in-service for referring physicians to acquaint them with the theory behind the therapy protocol, the specific functioning of the device, and the patient entrance criteria for the study. At the same time, long lead-time parts for the study devices would be ordered, followed by assembly and device quality checks in task 4. Once the physicians are fully familiar with the device and the study, patients that are recommended by the participating physicians will be contacted in task 3. Patient information kits will be sent to them describing the purpose and protocol of the study. Follow-up phone calls will be made to answer any questions and ascertain their willingness to participate in the study and to schedule physician appointments for those that choose to participate. Just before beginning of the study, an extensive in-service session will be conducted for the therapist that will be conducting the patient evaluations and training. Task 6 is the preparation of study materials such as patient evaluation forms, individual patient study binders, and schedule charts. Task 7 is the therapy portion of the study. One patient a day will be scheduled with Dr.

Kwasnica on Monday, Wednesday, and Friday. Immediately following the physician evaluation, each patient will start the program under the direction of Deborah Taylor, OTR. In the second week of the study the therapist will see one starting patient and one follow-up patient on Monday, Wednesdays and Fridays. The therapist will see one start patient and two follow-up patients MWF on weeks 3, 4, 5, 7, and 8. In weeks 6 (Labor Day) and 9 (the final start week) the therapist will see six and eight patients respectively. In weeks 10 and 11 the final follow-up measurements will be made. Task 8 is the time period for completion of individual therapies. Upon completion of the protocol, the therapist will compile the downloaded data from the device and assemble all of the performance data and assign a confidential code number. Dr. Kwasnica and Ms. Taylor will review the study binder and provide it for data analysis. In task 9 the data will be analyzed as the patients are completed and a final summary prepared. This time line assures that all the 25 patients including prospective drop-outs can be recruited and accommodated in the 6 month time frame and this can only be done by us taking a proactive role to assure that all equipment and relevant supplies are gathered and in place before the official start date of the 6-month award. A final report addressing the feasibility of the device, device changes suggested by the results, and protocol changes suggested for the Phase II study. Assuming feasibility is demonstrated, an application for Phase II funding will be prepared for April 1, 2003, submission.

Table I Gantt Chart

ID	Task Name	Q2 '02			Q3 '02			Q4 '02			Q1 '03		
		Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar
1	NIH Early Funding Request												
2	Physician In-Service												
3	Patient Recruitment												
4	Device Manufacture												
5	Prepare Study Materials												
6	Therapist In-Service												
7	Patient Enrolment												
8	Completed Treatments												
9	Data Analysis												
10	Final Report Preparation												
11	Phase II Proposal Submittal												

E. HUMAN SUBJECTS

Involvement of Human Subjects: The purpose of the device under evaluation in this proposal is to facilitate the application of concentrated practice for stroke patients. Numerous studies, most notably by Taub and Wolf, have provided this therapy through one-on-one contact with physical therapists. In all of these studies there is no reason to believe that this intervention provides selective benefits (or limitations) based upon gender or racial attributes. In this study the gender and minority status will be recorded and reported for all patients. The patients identified by the participating physicians have the following demographics: 3 female and 4 male Hispanic or Latino; 7 female and 11 male not Hispanic or Latino; 1 male American Indian; 1 female and 3 male Black or African Americans; 9 female and 11 male of the White race. No Asian or Pacific Islanders were identified in the patient pool. The subjects of this pilot study roughly represent the population mixture of Maricopa County. The percentage of males in the study, 60%, is higher than the slightly less than 50% in the overall population. The study has 28% Hispanics compared to 24.5% in the population. The respective study and population percentages of the races are: Black or African American 16% versus 3.7%; Asian Native Hawaiian or other Pacific Islander 0% versus 2.3%; Native American 4% versus 2.0%. The small size and short time of this study make it difficult to exactly match the race, gender and ethnic background of the population. The numbers are so small that little meaningful statistical

conclusions can be made although physiological and functional performance will be reported for these categories. Children less than 18 years of age are excluded because an immature nervous system may respond differently to this therapy than a mature one and the low number of young patients available for this short study.

Human Research Material: All subjects will be individuals who have sustained a stroke 3 months prior to enrollment in this clinical trial. Subjects will be excluded if they do not meet our lowest level of minimal motor criteria and: 1) have a score of less than 24 on the Folstein Mini-Mental State Examination; 2) have sustained a stroke less than 3 months prior to the initiation of therapy; 3) are less than 18 years old (given an immature nervous system may respond differently to this type of therapy than a mature nervous system); 4) show a clinical judgment of excessive frailty or lack of stamina; 5) have serious uncontrolled medical conditions; 6) demonstrate excessive pain in any joint of the more affected extremity that could limit ability to cooperate with the intervention, as judged by the examining clinician; 7) have passive range of motion less than 45 degrees for: abduction, flexion or external rotation at shoulder, or pronation of forearm; or greater than 30 degrees flexion contracture at any finger joint (patients who pass the motor criteria specified above do not tend to have the type of pain or limitation of movement that would exclude them from treatment); 8) cannot stand independently for 2 min., transfer independently to and from the toilet or perform sit-to-stand;

Obtaining Past Data: All past data will be in the form of medical records and radiographic materials designed to confirm the diagnosis, site and type of lesion. These data will be obtained specifically for research purposes. The identity of patients and their medical records will be protected. Patient participants in this trial will receive codes to protect their identity throughout the study.

Recruitment of subjects: A majority of the patients will come from the practice of Dr. Kwasnica. Patients will also be recruited from Dr. Kwasnica's partners and from Rhodes Rehabilitation Hospital in Mesa (Dr. Kosak), and Boswell Medical Center in Sun City, AZ (Dr. Lachman). The patients will be referred to Dr. Kwasnica's facility for treatment. Dr. Kwasnica has identified 15 patients that meet the criteria. Dr. Kwasnica's partners, Drs. Kosak and Lachman have identified 5 each. Of these the physicians estimate that a total of 25 of these patients will participate in the study. All subjects will sign informed consents at the time of enrollment. These consent forms will be approved by the Institutional Review Board of St. Joseph's Medical Center. The information contained therein describes the study, its purpose and duration, appropriate contact personnel, risks and discomforts, benefits, etc.

Potential Risks: The physical risk involved with using this device is overextending a joint and causing soft tissue damage. Another risk is fatiguing the patient and causing anxiety. The risks involved with use of EMG electrodes are skin irritation. The only psychological risk might occur if a patient feels frustrated by their lack of progress. A control on this risk is that the patient has the right to drop out of the study at any time.

Minimization of Risk: The risk of overstretching a joint is controlled in several ways. There is a physical stop incorporated in the side bearing that prevents wrist extension over 60°degrees of extension. If the wrist is stopped by an obstruction, the force is limited by the low stiffness of the air muscle actuator. Also, if the torque measured by the extension bar exceeds 8 newton meters (the resistive torque of the finger and wrist flexors), the air is exhausted and the device shut down. A panic button is also provided for easy access by the unaffected hand that will also exhaust the air muscle and shut the device down if the patient is feeling any discomfort, fatigue or anxiety.

Reasonableness of Risk: As noted above, effective means of controlling the risks are designed into the device. When one realizes that the potential benefit can be substantially enhanced function in real world

activities and improved quality of life beyond that achieved during the early rehabilitation interval, the risks are not significant.

FDA Approval: It is our opinion that this device is not a significant risk device and that only IRB approval is required. We will submit the protocol, a description of the device, a patient consent form, and an evaluation of the hazards involved in use of the device and how we are controlling these hazards to the Barrow Neurological Institute/St. Joseph Medical Center IRB.

F. VERTEBRATE ANIMALS

Not applicable.

G. LITERATURE CITED

1. H.I. Krebs, B.T. Volpe, M.L. Aisen, N. Hogan, "Increasing Productivity and Quality of Care: Robot-aided Neuro-rehabilitation", Journal of Rehabilitation Research and Development, Vol. 37, No. 6, Nov/Dec, 2000, PP 630-652.
2. E. Taub, G. Uswatte, R. Pidikiti, "Constraint-Induced Movement Therapy: A New Family of Techniques with Broad Application to Physical Rehabilitation – A Clinical Review", Journal of Rehabilitation Research an Development, Vol. 36, No. 3, July 1999, pp 237-251.
3. G.E. Gresham, "Post-stroke Rehabilitation", U.S. Dept of Health and Human Services, Public Heath Service, Agency for Health Care Policy and Research, May 1995, AHCPR publication # 95-0662.
4. E. Taub, "Guest Editorial: New Discovery Equals Change in Clinical Practice", Journal of Rehabilitation Research & Development, Vol. 36, No. 3, July 1999, pp. vii-viii.
5. P. Bach-y-Rita, E. Wicab Bach-y-Rita, "Biological and Psychosocial Factors in Recovery from Brain Damage in Humans", Canadian Journal of Psychology, 1990, Vol. 44 pp. 148-65.
6. P. Bach-y-Rita, "Recovery from Brain Injury", Journal of Neurological Rehabilitation, 1993, Vol. 6, pp. 191-9.
7. S.I. Franz, M.E. Scheetz, A.A. Wilson, "The Possibility of Recovery of Motor Functioning in Long-standing Hemiplegia", Journal of the American Medical Association, 1915, Vol. 65, pp. 2150-4.
8. S.L. Wolf, S.A. Binder-Macleod, "Electromyographic Biofeedback Applications to the Hemiplegic Patient: Changes in Upper Extremity Neuromuscular and Functional Status", Physical Therapy, 1983, Vol. 63, pp. 1393-403.
9. S.L. Wolf, "Electromyographic Biofeedback Applications to Stroke Patients: A Critical Review", Physical therapy, 1983, Vol. 63, pp. 1448-55.
10. J.V. Basmajian, E.M. Regenos, M.P. Baker, "Rehabilitation Stroke Patients with Biofeedback," Geriatrics, 1972, Vol. 32, pp. 85-8.
11. B.V. Basmajian, C.G. Kukulka, M.G. Narayan, K. Takebe, "Biofeedback Treatment of Foot-drop After Stroke Compared with Standard Rehabilitation Technique: Effects on Voluntary Control and Strength", Archives of Physical Medical Rehabilitation, 1975, Vol. 561, pp. 231-6.
12. R. Balliet, B. Levy, K.M.T. Blood, "Upper Extremity Sensory Feedback Therapy in Chronic Cerebrovascular Inpatients with Impaired Expressive Aphasia and Auditory Comprehension," Archives of Physical Medical Rehabilitation, 1986, Vol. 61, pp. 301-10.

13. C. Butefisch, H. Hummelsheim, P. Kenzler, K-H. Mauritz, "Repetitive Training of Isolated Movements Improves the Outcome of Motor Rehabilitation of the Centrally paretic Hand," Journal Neurological Science, 1995, Vol. 130, pp. 59-68.
14. S. Hesse, C. Bertelt, A. Schaffrin, M.S. Malezic, K-H. Mauritz, "Restoration of Gait in Nonambulatory Hemiparetic Patients by Treadmill Training with Partial Body-weight Support", Archives of Physical Medicine and Rehabilitation, 1994, Vol 75, pp. 1087-93.
15. S. Hesse, C. Bertelt, M.T. Jahnke, "Treadmill Training with Partial Body Weight Support Compared with Physiotherapy in Nonambulatory Hemiparetic Patients", Stroke, 1995, Vol. 26, pp. 976-81.
16. E. Taub, J.E. Crago, G. Uswatte, "Constraint-Induced Movement Therapy: A New Approach to Treatment in Physical Rehabilitation", rehabilitative Psychology, 1998, Vol43, pp. 152-70.
17. D. Reinkensmeyer, L.E. Kahn, M. Averbunch, A. McKenna-Cole, B.D. Schmit, W. Zev Rymer, "Understanding and Treating Arm Movement Impairment after Chronic Brain Injury: Progress with the ARM Guide," Journal of Rehabilitation Research and Development Vol. 27, No. 6, Nov/Dec 2000, pp. 653-662.
18. N. Hogan, "Guest Editorial: Rehabilitation Applications of Robotic Technology", Journal of Rehabilitation Research and Development, Vol. 37, No. 6, Nov/Dec 2000, pp. ix-x.
19. H.F. Schulte, Jr., "The Characteristics of the McKibben Artificial Muscle", in The Application of External Power in Prosthetics and Orthotics, Publication 874 National Academy of Sciences – National Research Council, Washington, D.C., 1961, pp.94-115.
20. V.L. Nickel, J. Perry, A.L. Garrett, "Development of Useful Function in the Severely Paralyzed Hand", Journal of Bone and Joint SurgeryVol. 45-A, No. 5, July 1963, pp. 933-952.
21. C-P. Chou, B. Hannaford, "Measurement and Modeling of McKibben Pneumatic Artificial Muscles", IEEE Transactions on Robotics and Automation, Vol. 12, No. 1, Feb. 1996, pp. 90-102.
22. G. K. Klute, B. Hannaford, "Modeling Pneumatic McKibben Artificial Muscle Actuators: Approaches and Experimental Results", ASME Journal of Dynamic Systems, Measurement, and Control, Nov. 1998.
23. G.K. Klute, J.M. Czeniecki, B. Hannaford, "McKibben Artificial Muscles: Pneumatic Actuators with Biomechanical Intelligence", IEEE/ASME 1999, International Conference on Advanced Intelligent Mechantronics (AIM '99), Sept 19-22, 1999.
24. C-P Chou, B. Hannaford, "Static and Dynamic Characteristics of McKibben Pneumatic Artificial Muscles", 1994.
25. G.K. Klute, B. Hannaford, "Fatigue Characteristics of McKibben Artificial Muscle Actuators", University of Washington.
26. G. Francisco, J. Chae, H. Chawla, S. Kirshblum, R. Zorowitz, G. Lewis, S. Pang, "Electromyogram-Triggered Neuromuscular Stimulation for Improving the Arm Function of Acute Stroke Survivors: A Randomized Pilot Study", Arch Phys Med Rehabil, Vol. 79, May 1998, pp. 570-575.
27. J. Cauraugh, K. Light, S. Kim, M. Thigpen, A. Behrman, "Chronic Motor Dysfunction After Stroke", Recovering Wrist and Finger Extensiion by Electromyography-Triggered Neuromuscular Stimulation", Stroke, 2000, Vol. 31, pp. 1360-1364.
28. G.H. Kraft, S.S. Fitts, M.C. Hammond, "Techniques to Improve Function of the Arm and Hand in Chronic Hemiplegia", Arch Phys Med Rehabil, Vol. 73, March 1992, pp. 220-227.
29. M. Glanz , S. Klawansky, W. Stason, C. Berkey, T. Chalmers, "Functional Electrostimulation in Poststroke Rehabilitation: A meta-analysis of the Randomized controlled Trials", Archives of Physical Medicine and Rehabilitation, 1996 Vol.77, pp.549-553.

30. J.D. Moreland, M. Thomson, A.R. Fuoco, "Electromyographic Biofeedback to Improve Lower Extremity Function After Stroke: A Meta-Analysis", Arch Phys Med Rehabil, Vol. 79, Feb. 1998, pp. 134-140.
31. S.L. Wolf, D.E. Lecraw, L.A. Barton, B.B. Jann, "Forced Use of Hemiplegic Upper Extremities to Reverse the Effect of Learned Nonuse Among Chronic Stroke and Head-Injured Patients", Experimental Neurology, Vol. 104, 1989, pp. 125-132.
32. E. Taub, N.E. Miller, T.A. Novack, E.W. Cook, W.C. Fleming, C.S. Nepomuceno, J.S. Connell, J.E. Crago, "Technique to Improve Chronic Motor Deficit After Stroke", Arch Phys Med Rehabil, Vol. 74, April 1993, pp. 347-354.
33. http://www.shadow.org.uk
34. J. Chae, R. Hart, "Comparison of Discomfort Associated with Surface and Percutaneous Intramuscular Electrical Stimulation for Persons with Chronic Hemiplegia", Am J Phys Med Rehabil, 1998, Nov-Dec, Vol. 77 No. 6, pp. 516-22.
35. C.G. Ostendorf, S.L. Wolf, "The effect of forced use of upper extremity of a hemiplegic patient on changes in function: a single case design", Phys Ther 62:1022-1028, 1981.
36. S.L. Wolf, "Forced use of a paretic upper extremity may facilitate function in select chronic head injured patients," Research Forum 1:4-5, 1986.
37. Extremity Constraint-Induced Training Evaluation (EXCITE) trial, Steven L. Wolf, Ph.D., FAPTA, Principal Investigator, NCMRR,HD 37606.
38. S.L. Wolf, P.A. Catlin, M. Ellis, A. Link, B. Morgan, A. Piacentino, "Assessing the Wolf motor function test as an outcome measure for research with patients post-stroke", Stroke, 32:1635-39, 2001.
39. P.M. Duncan, SM Lai, "Stroke Recovery", Topics in Stroke Rehabilitation, Vol 4, No. 3, pp. 51-58, 1997.

H. CONTRACTUAL ARRANGEMENTS

Dr. Wolf is participating at no cost with the anticipation that this study will lead to a device that is supportive of the treatments being studied in the EXCITE trial.

The applicant organization and St. Joseph's Medical Center/ St. Joseph's Medical Center are prepared to establish in writing the required contractual agreements whereby the clinical institutions will provide physician and therapist services as described in this proposal. The cost of providing these services is included in the budget of this proposal. The applicant organization will pay the clinical institution charges based on an agreed upon per patient fee.

I. CONSULTANTS

An Advisory Board for the project will provide advice and guidance on clinical issues, engineering, and product development. The members of the Advisory Board are:

- Dr. Steven Wolf, Ph.D., Professor of Rehabilitation Medicine at Emory University. Dr. Wolf is the principal investigator of a randomized national clinical trial to explore the effect of forced use therapy on patients who have sustained a stroke. He will be advising on the treatment and evaluation protocols and provide general guidance on the treatment of stroke patients.
- Dr. Jiping He, an Associate Professor of Bioengineering at Arizona State University. Dr. He is Director of the NSF Neuromuscular Control Laboratory at ASU and has extensive experience with neuromuscular stimulation and control. He will consult on neurostimulation and EMG sensing and control issues.

- Deborah Koeneman has a MS degree in Bioengineering from ASU. She has worked for the Food and Drug Administration in regulation of Medical Devices. She currently is Director of Regulatory Affairs for OrthoLogic Corporation. She will consult on clinical trial, regulatory, and quality assurance issues.
- Don Herring, an Assistant Professor of Industrial Design at ASU, will consult on human factors, industrial design, and attachment design.
- Cristobel Eblen, Ph.D., Cris is a psychologist with experience in designing patient evaluation studies and questionnaires and performing statistical analyses.

Principal Investigator/Program Director *(Last, first, middle):* Koeneman, James, Bryant

CHECKLIST

TYPE OF APPLICATION *(Check all that apply.)*

☐ NEW application. *(This application is being submitted to the PHS for the first time.)*

☒ SBIR Phase I ☐ SBIR Phase II: SBIR Phase I Grant No. _____ ☐ SBIR Fast Track

☐ STTR Phase I ☐ STTR Phase II: STTR Phase I Grant No. _____ ☐ STTR Fast Track

☒ REVISION of application number: 1 R43 HD41805-01

(This application replaces a prior unfunded version of a new, competing continuation, or supplemental application.)

☐ COMPETING CONTINUATION of grant number: _____

(This application is to extend a funded grant beyond its current project period.)

INVENTIONS AND PATENTS *(Competing continuation appl. and Phase II only)*

☐ No ☐ Previously reported

☐ Yes. If "Yes," ☐ Not previously reported

☐ SUPPLEMENT to grant number: _____

(This application is for additional funds to supplement a currently funded grant.)

☐ CHANGE of principal investigator/program director.

Name of former principal investigator/program director: _____

☐ FOREIGN application or significant foreign component.

1. PROGRAM INCOME ***(See Instructions.)***

All applications must indicate whether program income is anticipated during the period(s) for which grant support is request. If program income is anticipated, use the format below to reflect the amount and source(s).

Budget Period	Anticipated Amount	Source(s)
	0	

2. ASSURANCES/CERTIFICATIONS ***(See instructions.)***

The following assurances/certifications are made and verified by the signature of the Official Signing for Applicant Organization on the Face Page of the application. Descriptions of individual assurances/ certifications are provided in Section III. If unable to certify compliance, where applicable, provide an explanation and place it after this page.

•Human Subjects; •Research Using Human Pluripotent Stem Cells• •Research on Transplantation of Human Fetal Tissue •Women and Minority Inclusion Policy •Inclusion of Children Policy• Vertebrate Animals• •Debarment and Suspension; •Drug- Free Workplace *(applicable to new [Type 1] or revised [Type 1] applications only)*; •Lobbying; •Non-Delinquency on Federal Debt; •Research Misconduct; •Civil Rights (Form HHS 441 or HHS 690); •Handicapped Individuals (Form HHS 641 or HHS 690); •Sex Discrimination (Form HHS 639-A or HHS 690); •Age Discrimination (Form HHS 680 or HHS 690); •Recombinant DNA and Human Gene Transfer Research; •Financial Conflict of Interest (except Phase I SBIR/STTR) •STTR ONLY: Certification of Research Institution Participation.

3. FACILITIES AND ADMINSTRATIVE COSTS (F&A)/ INDIRECT COSTS. See specific instructions.

☐ DHHS Agreement dated: _____ ☒ No Facilities And Administrative Costs Requested.

☐ DHHS Agreement being negotiated with _____ Regional Office.

☐ No DHHS Agreement, but rate established with _____ Date _____

CALCULATION* *(The entire grant application, including the Checklist, will be reproduced and provided to peer reviewers as confidential information. Supplying the following information on F&A costs is optional for for-profit organizations.)*

a. Initial budget period:	Amount of base $		x Rate applied		% = F&A costs	$	
b. 02 year	Amount of base $		x Rate applied		% = F&A costs	$	
c. 03 year	Amount of base $		x Rate applied		% = F&A costs	$	
d. 04 year	Amount of base $		x Rate applied		% = F&A costs	$	
e. 05 year	Amount of base $		x Rate applied		% = F&A costs	$	
					TOTAL F&A Costs $		

*Check appropriate box(es):

☐ Salary and wages base ☐ Modified total direct cost base ☐ Other base *(Explain)*

☐ Off-site, other special rate, or more than one rate involved *(Explain)*

Explanation *(Attach separate sheet, if necessary.):*

4. SMOKE-FREE WORKPLACE ☒ Yes ☐ No *(The response to this question has no impact on the review or funding of this application.)*

EMORY UNIVERSITY SCHOOL OF MEDICINE
CENTER FOR REHABILITATION MEDICINE
1441 Clifton Road, N.E. Atlanta, Georgia 30322

DEPARTMENT OF
REHABILITATION MEDICINE

(404) 712-5507

November 26, 2001

Mr. James B Koeneman, President
Kinetic Muscles, Inc.
1949 East Broadway Road
Suite D
Tempe, AZ 85282

Dear Jim:

I have read your revised SBIR proposal, "Development of a Massed Practice Stroke Therapy Device"(1 R43 HD41805-01) regarding the application of your combined force feedback and EMG biofeedback pneumatic muscle instrumentation to facilitate improved movement and function in the wrists and digits of patients who have sustained a stroke but in whom movement initiation into extension exists. The refinements in the device construct and in the implementation/analysis plan are excellent.

As you know, I have spent considerable time researching criteria for the use of EMG biofeedback applied to the upper extremities of patients after stroke. I have also done considerable work in the area of "forced use" or "constraint induced movement therapy" among stroke patients and currently am PI on the NIH funded EXCITE (EXtremity Constraint Induced Therapy Evaluation) national clinical trial. I will be more than honored to serve as a consultant to your project. As you know I am very concerned that the potential to use multi-modal (muscle and force) physiological feedback be made optimal and researched with extreme vigor. I believe that your device will assist in the delivery of excellent product development and well-performed research. I have met many of your staff and am acutely aware of their commitment to this project.

Good luck with your efforts. If I can assist in any way during the final preparation of this proposal, please feel free to call upon me.

Steven L. Wolf

STEVEN L. WOLF, Ph.D., FAPTA, PT
Professor, Department of Rehabilitation Medicine
Professor of Geriatrics, Department of Medicine
Associate Professor, Department of Cell Biology
Director, Program in Restorative Neurology (PROREN)
Emory University School of Medicine

Barrow Neurological Institute®

St. Joseph's Hospital and Medical Center

June 1, 2001

To whom it may concern:

This letter shall serve as a letter of support for the Small Business Innovation Research grant titled "Development of a Massed Practice Stroke Therapy Device." I am pleased to be asked to participate in the opportunity to engineer a device that may assist patients in applying the principles of massed practice in their stroke recovery.

As Director of Brain Injury Rehabilitation at Barrow Neurological Institute, I have the background to be able to participate in such research. I am looking forward to collaboration in this study.

Sincerely,

C. Kwasnica MD

Christina Kwasnica M.D.
Attending Physiatrist
Barrow Neurological Institute
St. Joseph's Hospital & Medical Center
Phoenix, AZ 85013